

Table.S1: Literature overview of molecular, immunological and histopathological findings in BME..

Reference	Year	Study Design	disease	location	<i>in vivo</i> / <i>in vitro</i>	species	gene/ molecule	increased/ decreased	treatment	comment
1	2003	Case report	Subchondral insufficiency fracture (SIF)	Radiological, Histology	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	n.a.	dense irregular, discontinued trabeculae
2	2017	Animal model	Bone marrow lesion	Radiological, Histology	<i>in vivo</i>	Oryctolagus cuniculus	n.a.	n.a.	n.a.	Biomechanical BME induction and MRI
3	2018	Cohort Study	Spondyloarthropathy	Serum	<i>in vivo</i>	Homo sapiens	GDF15	increased	n.a.	
4	2019	Interventional Study	Spondyloarthropathy	Serum	<i>in vivo</i>	Homo sapiens	DKK1	decreased	TNF antibody	
5	2011	Genetic animal model	Spondyloarthropathy	Radiological, Histology	<i>in vivo</i>	Mus musculus	n.a.	n.a.	n.a.	Biomechanical BME induction and MRI, TNF is essential for the induction and maintenance of BME, increased vascularity and cellularity
6	2010	Genetic animal model	Spondyloarthropathy	Radiological, Histology	<i>in vivo</i>	Mus musculus	n.a.	n.a.	n.a.	Biomechanical BME induction and MRI, no significant increase of BME in TNFtg mice, but sig. Increase of osteoclasts and vascularity
7	2013	Cohort Study	Axial psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis	Serum	<i>in vivo</i>	Homo sapiens	HLA-B27	increased	n.a.	HLA-B27 positive correlation to BME
8	2006	Case series	Ankylosing spondylitis	Histology	<i>in vivo</i>	Homo sapiens	CD3	increased	n.a.	T cells
							CD4	increased		T cells
							CD8	increased		T cells
							CD20	increased		B cells
							CD34	increased		vessels
HLA-B27	increased									
9	2012	Cohort Study	Ankylosing spondylitis	Serum	<i>in vivo</i>	Homo sapiens	MMP3	increased	n.a.	
10	2017	Cohort Study	Undifferentiated arthritis	Serum, Synovia	<i>in vivo</i>	Homo sapiens	Galectin-3 PIIANP	increased decreased	n.a.	
11	2016	Case series	Rheumatoid arthritis	Radiologic, Serum	<i>in vivo</i>	homo sapiens	anti-citrullinated protein antibodies (ACPA)	increased	n.a.	
							rheumatoid factor (RF)	increased		
							anti-carbamylated protein (anti-CarP)	increased		
12	2018	Genetic animal model	Rheumatoid arthritis	Histology	<i>in vivo</i>	Mus musculus	CD3	increased	n.a.	Tyro3/Axl/Mertk-deficient mice, T cells
							CD19	increased		B cells
							ADGRE1	increased		macrophages
13	2007	Genetic animal model, Human sample	Osteoarthritis	Radiological	<i>in vivo</i>	Homo sapiens Cavia porcellus	n.a.	n.a.	n.a.	Reduced tibia perfusion

14	2005	Animal model	Osteoarthritis	Radiological	<i>in vivo</i>	Canis lupus familiaris	n.a.	n.a.	n.a.	
15	2008	Case series	Osteoarthritis	Radiological, Histology	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	n.a.	abnormal swollen adipocytes, healing micro-fractures, cyst formation, thickened subchondral plate/subchondral sclerosis
16	2019	Cohort study	Osteoarthritis	Radiological, Serum	<i>in vivo</i>	Homo sapiens	RETN	increased	n.a.	
17	2019	Cohort study	Osteoarthritis	Radiological, Histology	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	n.a.	Bone morphology changes in the anterior-medial (AM) region
18	2016	Cohort study	Osteoarthritis	Radiological, Histology	<i>in vivo</i>	Homo sapiens	vWF CD31	increased increased	n.a.	increased bone turnover, increased vascularity, reduced fat
19	2019	Animal model	Osteoarthritis	Radiological, Synovia, Histology, <i>In vitro</i> experiments	<i>in vivo</i>	Mus musculus	CD11b TRAP CD254	increased increased increased	n.a.	collagen-AB induced OA, decrease of trabecula, increase of B/T cells
20	2019	Interventional study	Osteoarthritis	Radiological	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	vitamine D	no effect
21	2014	Interventional study	Osteoarthritis	Radiological, Urine	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	glucosamine	no treatment benefit
22	2004	Case series	Chondroblastoma	Radiological, Histology	<i>in vivo</i>	Homo sapiens	Cyclooxygenase-2	increased	n.a.	
23	2008	Animal model	Avascular necrosis	Radiological, Histology	<i>in vivo</i>	Oryctolagus cuniculus	VEGF	decreased	n.a.	corticosteroid injection, reduced bone
24	2008	Case series	Osteonecrosis	Serum	<i>in vivo</i>	Homo sapiens	Kininogen variant 1 Complement factor C3 precursor Complement factor H Apolipoprotein A-IV precursor Antithrombin III chain B Gelsolin isoform α precursor	increased increased increased decreased decreased decreased	n.a.	
25	2018	Cohort study	Avascular necrosis	Serum	<i>in vivo</i>	Homo sapiens	TNF IL6	decreased decreased	hyperbaric oxygen	
26	2009	Case Report	Hypophosphatasia	Radiological, Histology	<i>in vivo</i>	Homo sapiens	ALPL	SNP	n.a.	bone necrosis, marrow fibrosis
27	2011	Case Report	Hypophosphatasia	Radiological, <i>in vitro</i> assays	<i>in vivo/vitro</i>	Homo sapiens	ALPL	SNP	n.a.	
28	2003	Cohort study	Bone marrow edema syndrome	Radiological, Histology, Serum	<i>in vivo</i>	Homo sapiens	osteocalcin bone ALP C-terminal cross-linking telopeptide PIIANP	increased increased increased increased	n.a.	mean bone-to-serum ratio
29	2017	Case series	Bone marrow edema syndrome	Radiological, Serum	<i>in vivo</i>	Homo sapiens	25(OH)D	decreased	n.a.	

30	2002	Case series	Bone marrow edema syndrome	Radiological, Serum	<i>in vivo</i>	Homo sapiens	lipoprotein (a) ApoA1 ApoB	decreased increased increased	n.a.	
31	2000	Case series	Bone marrow edema syndrome	Serum	<i>in vivo</i>	Homo sapiens	lipoprotein (a)	increased	n.a.	
32	2007	Case report	Regional transient osteoporosis	Radiological	<i>in vivo</i>	Homo sapiens	vitamin C	decreased	n.a.	no reduced perfusion
33	2019	Cross-Sectional study	Bone marrow edema syndrome	Radiological, Serum	<i>in vivo</i>	Homo sapiens	bone-alkaline phosphatase (BAP) type I procollagen N-terminal propeptide (PINP) cross-linked N-telopeptide of type I collagen (NTx) tartrateresistant acid phosphatase-5b (TRACP-5b) pentosidine	increased increased increased increased increased	n.a.	decreased bone mineral density
34	2013	Case series	Bone marrow edema syndrome	Radiological, Serum	<i>in vivo</i>	Homo sapiens	lipoprotein (a) ApoA1 ApoB	increased Increased increased	iloprost	
35	2005	Case series	hydroxyapatite deposition disease	Radiological	<i>in vivo</i>	Homo sapiens	n.a.	n.a.	n.a.	underlying the enthesis

n.a.: not applicable

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